

Complete Summary

GUIDELINE TITLE

(1) Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). (2) Update: influenza activity -- United States and worldwide, May 22-September 3, 2005, and 2005-06 season vaccination recommendations. (3) High levels of adamantane resistance among influenza A (H3N2) viruses and interim guidelines for use of antiviral agents --- United States, 2005--06 influenza season.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). High levels of adamantane resistance among influenza A (H3N2) viruses and interim guidelines for use of antiviral agents--United States, 2005-06 influenza season. MMWR Morb Mortal Wkly Rep 2006 Jan 20; 55(2): 44-6. [9 references] [PubMed](#)

Centers for Disease Control and Prevention (CDC). Tiered use of inactivated influenza vaccine in the event of a vaccine shortage. MMWR Morb Mortal Wkly Rep 2005 Aug 5; 54(30): 749-50. [4 references] [PubMed](#)

Centers for Disease Control and Prevention (CDC). Update: influenza activity--United States and worldwide, May 22-September 3, 2005, and 2005-06 season vaccination recommendations [published erratum in MMWR Morb Mortal Wkly Rep 2005 Sep 23; 54(37): 935]. MMWR Morb Mortal Wkly Rep 2005 Sep 16; 54(36): 899-902. [10 references] [PubMed](#)

Centers for Disease Control and Prevention (CDC). Update: influenza vaccine supply and recommendations for prioritization during the 2005-06 influenza season. MMWR Morb Mortal Wkly Rep 2005 Sep 2; 54(34): 850. [5 references] [PubMed](#)

Harper SA, Fukuda K, Uyeki TM, Cox NJ, Bridges CB. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2005 Jul 29; 54(RR-8): 1-40. [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline combined with the addended material, updates a previous version: Centers for Disease Control and Prevention. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2004 May 28; 53(RR-6): 1-40.

This guideline is updated annually for each upcoming influenza season.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Influenza

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Geriatrics
Infectious Diseases
Internal Medicine
Pediatrics
Pharmacology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To describe new findings regarding the resistance to adamantanes of influenza A viruses currently circulating in the United States and provide interim recommendations that these drugs not be used during the remainder of the 2005-06 influenza season (January 17, 2006 Addendum)
- To provide supplemental recommendations to the July 2005 guidelines issued by the Advisory Committee on Immunization Practices (ACIP) regarding the use of influenza vaccine and antiviral agents
- To update the 2004 recommendations by the ACIP

TARGET POPULATION

- Persons at increased risk for influenza-related complications (i.e., those aged ≥ 65 years with or without comorbid conditions, children aged 6 to 23 months, pregnant women, residents of long-term care facilities, and persons aged 2 to 64 years with certain comorbid conditions)
- Persons who live with or care for persons at high risk (e.g., health-care workers and household contacts who have frequent contact with persons at high risk and who can transmit influenza to those persons at high risk)
- Persons aged 50 to 64 years because this group has an elevated prevalence of certain chronic medical conditions
- Healthy persons 5 to 49 years (live attenuated influenza virus)
- Persons displaced by Hurricane Katrina (2005 Sep 16 addendum)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Annual immunoprophylaxis:

- Inactivated (i.e., killed-virus) trivalent influenza vaccine (FluZone® split virus, Fluvirin™, Fluarix™)
- Live attenuated influenza vaccine (FluMist™)

Both the inactivated and live, attenuated vaccines prepared for the 2005-2006 season will include:

- A/California/7/2004 (H3N2)-like (manufacturers may use the antigenically equivalent A/New York/55/2004 (H3N2) virus)
- A/New Caledonia/20/99 (H1N1)-like
- B/Shanghai/361/2002-like antigens (manufacturers may use the antigenically equivalent B/Jilin/20/2003 virus or B/Jiangsu/10/2003 virus)

2. Influenza-specific antiviral drugs* (zanamivir, oseltamivir)

*Note: Amantadine and rimantadine are no longer recommended. See the January 2006 addendum at the beginning of the "Major Recommendations" field for more information.

MAJOR OUTCOMES CONSIDERED

- Influenza-related morbidity and mortality rates
- Influenza-related hospitalization rates
- Cost effectiveness of influenza vaccination

- Side effects and adverse reactions of influenza vaccination and antiviral agents
- Rates of adamantane resistance among influenza A viruses (2006 Jan 17 addendum)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Influenza vaccination can reduce both health-care costs and productivity losses associated with influenza illness. Economic studies of influenza vaccination of

persons aged ≥ 65 years conducted in the United States have reported overall societal cost savings and substantial reductions in hospitalization and death. Studies of adults aged < 65 years have reported that vaccination can reduce both direct medical costs and indirect costs from work absenteeism. Reductions of 13 to 44 percent in health-care-provider visits, 18 to 45 percent in lost workdays, 18 to 28 percent in days working with reduced effectiveness, and 25 percent in antibiotic use for influenza-associated illnesses have been reported. One cost-effectiveness analysis estimated a cost of approximately \$60 to \$4,000/illness averted among healthy persons aged 18 to 64 years, depending on the cost of vaccination, the influenza attack rate, and vaccine effectiveness against influenza-like illness (ILI). Another cost-benefit economic study estimated an average annual savings of \$13.66/person vaccinated. In the second study, 78 percent of all costs prevented were costs from lost work productivity, whereas the first study did not include productivity losses from influenza illness. Economic studies specifically evaluating the cost-effectiveness of vaccinating persons aged 50 to 64 years are not available, and the number of studies that examine the economics of routinely vaccinating children with inactivated or live, attenuated vaccine are limited. However, in a study of inactivated vaccine that included all age groups, cost utility (i.e., cost per year of healthy life gained) improved with increasing age and among those with chronic medical conditions. Among persons aged ≥ 65 years, vaccination resulted in a net savings per quality-adjusted life year (QALY) gained and resulted in costs of \$23 to \$256/QALY among younger age groups. Additional studies of the relative cost-effectiveness and cost utility of influenza vaccination among children and among adults aged < 65 years are needed and should be designed to account for year-to-year variations in influenza attack rates, illness severity, and vaccine efficacy when evaluating the long-term costs and benefits of annual vaccination.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

January 17, 2006 Addendum

Notice from the National Guideline Clearinghouse (NGC) and the Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices (CDC, ACIP): On January 17, 2006, the CDC reported new findings regarding the resistance to adamantanes of influenza A viruses currently circulating in the United States and provided interim recommendations that these drugs not be used during the remainder of the 2005-2006 influenza season.

The high levels of resistance to amantadine and rimantadine detected among influenza A viruses tested during this season necessitate an interim change in

recommendations for the use of these drugs. On the basis of available antiviral testing results, CDC recommends that neither amantadine nor rimantadine be used for the treatment or chemoprophylaxis of influenza A infections in the United States for the remainder of the 2005-06 influenza season. During this period, oseltamivir or zanamivir should be prescribed if an antiviral medication is indicated for the treatment of influenza, or oseltamivir should be prescribed for chemoprophylaxis of influenza. On January 14, 2006, a CDC Health Alert (available at <http://www.cdc.gov/flu/han011406.htm>) with these recommendations was sent via the Health Alert Network (HAN) to state and local health officers, public information officers, epidemiologists, HAN coordinators, and clinician organizations.

Testing of influenza isolates for resistance to antivirals will continue throughout the 2005-06 influenza season, and recommendations will be updated as needed. These findings of adamantane resistance pertain to human influenza A (H3N2) viruses and not to avian influenza A (H5N1) viruses isolated from birds or humans in Asia or Europe.

Recommendations for the use of the oseltamivir and zanamivir have not changed. The U.S. Food and Drug Administration (FDA) recently extended chemoprophylaxis approval of oseltamivir to include children aged 1-12 years; previously, chemoprophylaxis approval had been limited to children aged ≥ 13 years.

When administered for treatment within 48 hours of illness onset, neuraminidase inhibitors can reduce the duration of uncomplicated influenza A and B illness by approximately 1 day when compared with placebo. Persons at high risk for serious complications from influenza can benefit most from neuraminidase inhibitors. CDC recommends that neuraminidase inhibitors be used as treatment for any person experiencing a potentially life-threatening influenza-related illness and for persons at high risk for serious complications from influenza. CDC recommends that oseltamivir be used as chemoprophylaxis for 1) persons who live or work in institutions caring for persons at high risk for serious complications from influenza infection in the event of an institutional outbreak and 2) persons at high risk for serious influenza complications if they are likely to be exposed to others infected with influenza. The U.S. Food and Drug Administration-approved indications for the use of neuraminidase inhibitors are available at <http://www.cdc.gov/flu/professionals/treatment>.

Annual influenza vaccination remains the primary means of preventing morbidity and mortality associated with influenza. Because the influenza season has only recently begun in many areas of the United States, persons for whom influenza vaccination is recommended should still be vaccinated.

Additional information regarding the prevention and control of influenza is available at <http://www.cdc.gov/flu>. New information will be provided at this website as it becomes available.

September 16, 2005 Addendum

Notice from the National Guideline Clearinghouse (NGC) and the Centers for Disease Control and Prevention, Advisory Committee on Immunization

Practices (CDC, ACIP): On September 16, 2005, the CDC issued updated recommendations for influenza immunization, taking into consideration potential uncertainties regarding vaccination production and including recommendations for persons displaced by Hurricane Katrina.

Influenza Vaccine Supply and Recommendations

Vaccination is the primary method for preventing influenza. For the 2005 to 2006 influenza vaccine, four manufacturers expect to provide influenza vaccine to the U.S. population. Sanofi Pasteur, Inc., projects production of up to 60 million doses of trivalent inactivated influenza vaccine (TIV). Chiron Corporation projects production of 18 to 26 million doses of TIV. GlaxoSmithKline, Inc. projects production of 8 million doses of TIV. MedImmune Vaccines, Inc., producer of the nasal-spray, live attenuated influenza vaccine (LAIV), projects production of approximately 3 million doses.

Because of the uncertainties regarding production of influenza vaccine, the exact number of available doses and timing of vaccine distribution for the 2005 to 2006 influenza season remain unknown. As a result, CDC recommends that only the following priority groups receive TIV before October 24, 2005:

- Persons aged ≥ 65 years with comorbid conditions
- Residents of long-term-care facilities
- Persons aged 2 to 64 years with comorbid conditions
- Persons aged ≥ 65 years without comorbid conditions
- Children aged 6 to 23 months
- Pregnant women
- Health-care personnel who provide direct patient care
- Household contacts and out-of-home caregivers of children aged < 6 months

These groups correspond to tiers 1A-1C in the previously published table of TIV priority groups in the event of vaccination supply disruption ([CDC. Tiered use of inactivated influenza vaccine in the event of a vaccine shortage. MMWR 2005;54:749-50](#)). Beginning October 24, 2005, influenza vaccine should be made available to all persons. Healthy persons aged 5 to 49 years who are not pregnant, including health-care workers who are not caring for severely immunocompromised patients in special-care units, can receive LAIV at any time.

Vaccination Recommendations for Persons Displaced by Hurricane Katrina

On September 6, 2005, CDC issued interim vaccination recommendations for persons displaced by Hurricane Katrina. Any displaced persons aged ≥ 6 months living in crowded group settings should be administered influenza vaccine; children aged ≤ 8 years should be administered 2 doses, at least 1 month apart, unless they have a documented record of a previous dose of influenza vaccine, in which case they should receive 1 dose of influenza vaccine.

July 29, 2005 Guidelines

Primary Changes and Updates in the Recommendations

The 2005 recommendations include five principal changes or updates:

- The Advisory Committee on Immunization Practices (ACIP) recommends that persons with any condition (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration be vaccinated against influenza (see "Target Groups for Vaccination" below).
- ACIP emphasizes that all health-care workers should be vaccinated against influenza annually, and that facilities that employ health-care workers be strongly encouraged to provide vaccine to workers by using approaches that maximize immunization rates.
- Use of both available vaccines (inactivated and live, attenuated influenza vaccine [LAIV]) is encouraged for eligible persons every influenza season, especially persons in recommended target groups. During periods when inactivated vaccine is in short supply, use of LAIV is especially encouraged when feasible for eligible persons (including health-care workers) because use of LAIV by these persons might considerably increase availability of inactivated vaccine for persons in groups at high risk.
- The 2005 to 2006 trivalent vaccine virus strains are A/California/7/2004 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Shanghai/361/2002-like antigens. For the A/California/7/2004 (H3N2)-like antigen, manufacturers may use the antigenically equivalent A/New York/55/2004 virus, and for the B/Shanghai/361/2002-like antigen, manufacturers may use the antigenically equivalent B/Jilin/20/2003 virus or B/Jiangsu/10/2003 virus (see "Influenza Vaccine Composition" in the original guideline document).
- The Centers for Disease Control and Prevention (CDC) and other agencies will assess the vaccine supply throughout the manufacturing period and will make recommendations preceding the 2005 to 2006 influenza season regarding the need for tiered timing of vaccination of different risk groups. In addition, CDC will publish ACIP recommendations regarding inactivated vaccine subprioritization (tiering) at a later date.

Recommendations for Using Inactivated and Live, Attenuated Influenza Vaccine (LAIV)

Both the inactivated influenza vaccine and LAIV can be used to reduce the risk for influenza. LAIV is approved for use among healthy persons aged 5 to 49 years. Inactivated influenza vaccine is approved for persons aged ≥ 6 months, including those with high-risk conditions (see following sections on inactivated influenza vaccine and live, attenuated influenza vaccine).

Target Groups for Vaccination

Persons at Increased Risk for Complications

Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for complications from influenza:

- Persons aged ≥ 65 years
- Residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions

- Adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma (hypertension is not considered a high-risk condition)
- Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus [HIV])
- Adults and children who have any condition (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration
- Children and adolescents (aged 6 months to 18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after influenza infection
- Women who will be pregnant during the influenza season
- Children aged 6 to 23 months

Persons Aged 50 to 64 Years

Vaccination is recommended for persons aged 50 to 64 years because this group has an increased prevalence of persons with high-risk conditions.

Persons Who Can Transmit Influenza to Those at High Risk

Persons who are clinically or subclinically infected can transmit influenza virus to persons at high risk for complications from influenza. Decreasing transmission of influenza from caregivers and household contacts to persons at high risk might reduce influenza-related deaths among persons at high risk. Evidence from two studies indicates that vaccination of health-care workers is associated with decreased deaths among nursing home patients, and hospital-based influenza outbreaks frequently occur where unvaccinated health-care workers are employed. Administration of LAIV has been demonstrated to reduce medically attended acute respiratory illness (MAARI) in contacts of vaccine recipients, and to reduce influenza-like illness (ILI)-related economic and medical consequences (such as work days lost and number of health-care provider visits). In addition to health-care workers, additional groups that can transmit influenza to high-risk persons and that should be vaccinated include:

- Employees of assisted living and other residences for persons in groups at high risk
- Persons who provide home care to persons in groups at high risk
- Household contacts (including children) of persons in groups at high risk

In addition, because children aged 0 to 23 months are at increased risk for influenza-related hospitalization, vaccination is recommended for their household contacts and out-of-home caregivers, particularly for contacts of children aged 0 to 5 months, because influenza vaccines have not been approved by the U.S. Food and Drug Administration (FDA) for use among children aged <6 months.

Healthy persons aged 5 to 49 years in these groups who are not contacts of severely immunosuppressed persons (see Live, Attenuated Influenza Vaccine

Recommendations) can receive either LAIV or inactivated influenza vaccine. All other persons in this group should receive inactivated influenza vaccine.

Health-Care Workers

All health-care workers should be vaccinated against influenza annually. Facilities that employ health-care workers are strongly encouraged to provide vaccine to workers by using approaches that maximize vaccination rates. This will protect health-care workers, their patients, and communities, and will improve prevention of influenza-associated disease and patient safety, and will reduce disease burden. Influenza vaccination rates among health-care workers should be regularly measured and reported. Although vaccination rates for health-care workers are typically <40 percent, with moderate effort, organized campaigns can attain higher rates of vaccination among this population. Physicians, nurses, and other workers in both hospital and outpatient-care settings, including medical emergency-response workers (e.g., paramedics and emergency medical technicians), should be vaccinated, as should employees of nursing home and chronic-care facilities who have contact with patients or residents.

Additional Information Regarding Vaccination of Specific Populations

Pregnant Women

Because of the increased risk for influenza-related complications, women who will be pregnant during the influenza season should be vaccinated. Vaccination can occur in any trimester. One study of influenza vaccination of approximately 2,000 pregnant women demonstrated no adverse fetal effects associated with influenza vaccine.

Healthy Young Children

Because children aged 6 to 23 months are at substantially increased risk for influenza-related hospitalizations, ACIP recommends vaccination of all children in this age group. ACIP continues to recommend influenza vaccination of persons aged ≥ 6 months who have high-risk medical conditions.

The current inactivated influenza vaccine is not approved by FDA for use among children aged <6 months, the pediatric group at greatest risk for influenza-related complications. Vaccinating their household contacts and out-of-home caregivers might decrease the probability of influenza infection among these children.

Beginning in March 2003, the group of children eligible for influenza vaccine coverage under the Vaccines for Children (VFC) program was expanded to include all VFC-eligible children aged 6 to 23 months and VFC-eligible children aged 2 to 18 years who are household contacts of children aged 0 to 23 months.

Persons Infected with HIV

Limited information is available regarding the frequency and severity of influenza illness or the benefits of influenza vaccination among persons with HIV infection. However, a retrospective study of young and middle-aged women enrolled in

Tennessee's Medicaid program determined that the attributable risk for cardiopulmonary hospitalizations among women with HIV infection was higher during influenza seasons than during the peri-influenza periods. The risk for hospitalization was higher for HIV-infected women than for women with other well-recognized high-risk conditions, including chronic heart and lung diseases. Another study estimated that the risk for influenza-related death was 9.4 to 14.6/10,000 persons with acquired immunodeficiency syndrome (AIDS) compared with 0.09 to 0.10/10,000 among all persons aged 25 to 54 years and 6.4 to 7.0/10,000 among persons aged ≥ 65 years. Other reports indicate that influenza symptoms might be prolonged and the risk for complications from influenza increased for certain HIV-infected persons.

Inactivated influenza vaccination has been demonstrated to produce substantial antibody titers against influenza among vaccinated HIV-infected persons who have minimal AIDS-related symptoms and high CD4+ T-lymphocyte cell counts. A limited, randomized, placebo-controlled trial determined that inactivated influenza vaccine was highly effective in preventing symptomatic, laboratory-confirmed influenza infection among HIV-infected persons with a mean of 400 CD4+ T-lymphocyte cells/mm³; a limited number of persons with CD4+ T-lymphocyte cell counts of <200 were included in that study. A nonrandomized study among HIV-infected persons determined that influenza vaccination was most effective among persons with >100 CD4+ cells and among those with <30,000 viral copies of HIV type-1/mL. Among persons who have advanced HIV disease and low CD4+ T-lymphocyte cell counts, inactivated influenza vaccine might not induce protective antibody titers; a second dose of vaccine does not improve the immune response in these persons.

One study determined that HIV RNA (ribonucleic acid) levels increased transiently in one HIV-infected person after influenza infection. Studies have demonstrated a transient (i.e., 2 to 4 week) increase in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-infected persons after vaccine administration. Other studies using similar laboratory techniques have not documented a substantial increase in the replication of HIV. Deterioration of CD4+ T-lymphocyte cell counts or progression of HIV disease have not been demonstrated among HIV-infected persons after influenza vaccination compared with unvaccinated persons. Limited information is available concerning the effect of antiretroviral therapy on increases in HIV RNA levels after either natural influenza infection or influenza vaccination. Because influenza can result in serious illness and because vaccination with inactivated influenza vaccine can result in the production of protective antibody titers, vaccination will benefit HIV-infected persons, including HIV-infected pregnant women.

Breastfeeding Mothers

Influenza vaccine is safe for mothers who are breastfeeding and their infants. Breastfeeding does not adversely affect the immune response and is not a contraindication for vaccination.

Travelers

The risk for exposure to influenza during travel depends on the time of year and destination. In the tropics, influenza can occur throughout the year. In the

temperate regions of the Southern Hemisphere, the majority of influenza activity occurs during April through September. In temperate climate zones of the Northern and Southern Hemispheres, travelers also can be exposed to influenza during the summer, especially when traveling as part of large organized tourist groups (e.g., on cruise ships) that include persons from areas of the world where influenza viruses are circulating. Persons at high risk for complications of influenza who were not vaccinated with influenza vaccine during the preceding fall or winter should consider receiving influenza vaccine before travel if they plan to:

- Travel to the tropics
- Travel with organized tourist groups at any time of year
- Travel to the Southern Hemisphere during April through September

No information is available regarding the benefits of revaccinating persons before summer travel who were already vaccinated in the preceding fall. Persons at high risk who receive the previous season's vaccine before travel should be revaccinated with the current vaccine the following fall or winter. Persons aged ≥ 50 years and persons at high risk should consult with their physicians before embarking on travel during the summer to discuss the symptoms and risks for influenza and the advisability of carrying antiviral medications for either prophylaxis or treatment of influenza.

General Population

In addition to the groups for which annual influenza vaccination is recommended, physicians should administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill with influenza or transmitting influenza to others should they become infected (the vaccine can be administered to children aged ≥ 6 months), depending on vaccine availability (see the section titled "Influenza Vaccine Supply" in the original guideline document). Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (e.g., those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

Comparison of LAIV with Inactivated Influenza Vaccine

Both inactivated influenza vaccine and LAIV are available to reduce the risk for influenza infection and illness. However, the vaccines also differ in key ways (see Table 3 in the original guideline document).

Major Similarities

LAIV and inactivated influenza vaccine contain strains of influenza viruses that are antigenically equivalent to the annually recommended strains: one influenza A (H3N2) virus, one A (H1N1) virus, and one B virus. Each year, one or more virus strains might be changed on the basis of global surveillance for influenza viruses and the emergence and spread of new strains. Viruses for both vaccines are grown in eggs. Both vaccines are administered annually to provide optimal protection against influenza infection (see Table 3 in original guideline document).

Major Differences

Inactivated influenza vaccine contains killed viruses, whereas LAIV contains live, attenuated viruses still capable of replication. LAIV is administered intranasally by sprayer, whereas inactivated influenza vaccine is administered intramuscularly by injection. LAIV is more expensive than inactivated influenza vaccine, although the price differential between inactivated vaccine and LAIV has decreased for the 2005 to 2006 season. LAIV is approved for use among healthy persons aged 5 to 49 years; inactivated influenza vaccine is approved for use among persons aged ≥ 6 months, including those who are healthy and those with chronic medical conditions (see Table 3 in the original guideline document).

Inactivated Influenza Vaccine Recommendations

Persons Who Should Not Be Vaccinated with Inactivated Influenza Vaccine

Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see the "Potential Harms" section in this summary for Side Effects and Adverse Reactions). Prophylactic use of antiviral agents is an option for preventing influenza among such persons. However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at high risk for complications from influenza can benefit from vaccine after appropriate allergy evaluation and desensitization. Information regarding vaccine components is located in package inserts from each manufacturer. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever do not contraindicate use of influenza vaccine, particularly among children with mild upper-respiratory-tract infection or allergic rhinitis.

Dosage

Dosage recommendations vary according to age group (see Table 4 in the original guideline document). Among previously unvaccinated children aged < 9 years, 2 doses administered ≥ 1 month apart are recommended for satisfactory antibody responses. If possible, the second dose should be administered before December. If a child aged < 9 years receiving vaccine for the first time does not receive a second dose of vaccine within the same season, only 1 dose of vaccine should be administered the following season. Two doses are not required at that time. Among adults, studies have indicated limited or no improvement in antibody response when a second dose is administered during the same season. Even when the current influenza vaccine contains one or more antigens administered in previous years, annual vaccination with the current vaccine is necessary because immunity declines during the year after vaccination. Vaccine prepared for a previous influenza season should not be administered to provide protection for the current season. Because of lack of vaccine efficacy data, ACIP does not recommend that a child receiving influenza vaccine for the first time be given the first dose of vaccine in the spring, followed by the second dose in the autumn of the same year.

Route

The intramuscular route is recommended for influenza vaccine. Adults and older children should be vaccinated in the deltoid muscle. A needle length ≥ 1 inch can be considered for these age groups because needles < 1 inch might be of insufficient length to penetrate muscle tissue in certain adults and older children.

Infants and young children should be vaccinated in the anterolateral aspect of the thigh. ACIP recommends a needle length of 7/8 to 1 inch for children aged < 12 months for intramuscular vaccination into the anterolateral thigh. When injecting into the deltoid muscle among children with adequate deltoid muscle mass, a needle length of 7/8 to 1.25 inches is recommended.

Side Effects and Adverse Reactions

When educating patients regarding potential side effects, clinicians should emphasize that 1) inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza; and 2) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination. (See the "Potential Harms" section in this summary for more information.)

Live, Attenuated Influenza Vaccine (LAIV) Recommendations

Using LAIV

LAIV is an option for vaccination of healthy persons aged 5 to 49 years, including health-care workers and other persons in close contact with groups at high risk and those wanting to avoid influenza. During periods when inactivated vaccine is in short supply, use of LAIV is encouraged when feasible for eligible persons (including health-care workers) because use of LAIV by these persons might increase availability of inactivated vaccine for persons in groups at high risk. Possible advantages of LAIV include its potential to induce a broad mucosal and systemic immune response, its ease of administration, and the acceptability of an intranasal rather than intramuscular route of administration.

Persons Who Should Not Be Vaccinated with LAIV

The following populations should not be vaccinated with LAIV:

- Persons aged < 5 years or those aged ≥ 50 years*
- Persons with asthma, reactive airways disease, or other chronic disorders of the pulmonary or cardiovascular systems; persons with other underlying medical conditions, including such metabolic diseases as diabetes, renal dysfunction, and hemoglobinopathies; or persons with known or suspected immunodeficiency diseases or who are receiving immunosuppressive therapies*
- Children or adolescents receiving aspirin or other salicylates (because of the association of Reye syndrome with wild-type influenza infection)*
- Persons with a history of Guillain-Barre Syndrome (GBS)
- Pregnant women*
- Persons with a history of hypersensitivity, including anaphylaxis, to any of the components of LAIV or to eggs

*These persons should receive inactivated influenza vaccine.

Close Contacts of Persons at High Risk for Complications from Influenza

Close contacts of persons at high risk for complications from influenza should receive influenza vaccine to reduce transmission of wild-type influenza viruses to persons at high risk. ACIP has not indicated a preference for inactivated influenza vaccine use by health-care workers or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g., persons with diabetes, persons with asthma taking corticosteroids, or persons infected with HIV) or for inactivated influenza vaccine use by health-care workers or other healthy persons aged 5 to 49 years in close contact with all other groups at high risk. Use of inactivated influenza vaccine is preferred for vaccinating household members, health-care workers, and others who have close contact with severely immunosuppressed persons (e.g., patients with hematopoietic stem cell transplants) during those periods in which the immunosuppressed person requires care in a protective environment. The rationale for not using LAIV among health-care workers caring for such patients is the theoretical risk that a live, attenuated vaccine virus could be transmitted to the severely immunosuppressed person. If a health-care worker receives LAIV, that worker should refrain from contact with severely immunosuppressed patients for 7 days after vaccine receipt. Hospital visitors who have received LAIV should refrain from contact with severely immunosuppressed persons for 7 days after vaccination; however, such persons need not be excluded from visitation of patients who are not severely immunosuppressed.

Personnel Who May Administer LAIV

Low-level introduction of vaccine viruses into the environment is likely unavoidable when administering LAIV. The risk for acquiring vaccine viruses from the environment is unknown but likely to be limited. Severely immunosuppressed persons should not administer LAIV. However, other persons at high risk for influenza complications may administer LAIV. These include persons with underlying medical conditions placing them at high risk or who are likely to be at risk, including pregnant women, persons with asthma, and persons aged ≥ 50 years.

LAIV Dosage and Administration

LAIV is intended for intranasal administration only and should not be administered by the intramuscular, intradermal, or intravenous route. LAIV must be thawed before administration. This can be accomplished by holding an individual sprayer in the palm of the hand until thawed, with subsequent immediate administration. Alternatively, the vaccine can be thawed in a refrigerator and stored at 2 degrees C to 8 degrees C for ≤ 24 hours before use. Vaccine should not be refrozen after thawing. LAIV is supplied in a prefilled single-use sprayer containing 0.5 mL of vaccine. Approximately 0.25 mL (i.e., half of the total sprayer contents) is sprayed into the first nostril while the recipient is in the upright position. An attached dose-divider clip is removed from the sprayer to administer the second half of the dose into the other nostril. If the vaccine recipient sneezes after administration, the dose should not be repeated.

LAIV should be administered annually according to the following schedule:

- Children aged 5 to 8 years previously unvaccinated at any time with either LAIV or inactivated influenza vaccine should receive 2 doses of LAIV (one dose equals 0.5 mL, divided equally between each nostril) separated by 6 to 10 weeks.
- Children aged 5 to 8 years previously vaccinated at any time with either LAIV or inactivated influenza vaccine should receive 1 dose of LAIV. They do not require a second dose.
- Persons aged 9 to 49 years should receive 1 dose of LAIV.

LAIV can be administered to persons with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infection with or without fever). However, if clinical judgment indicates nasal congestion is present that might impede delivery of the vaccine to the nasopharyngeal mucosa, deferral of administration should be considered until resolution of the illness.

Whether concurrent administration of LAIV with other vaccines affects the safety or efficacy of either LAIV or the simultaneously administered vaccine is unknown. In the absence of specific data indicating interference, following the ACIP general recommendations for immunization is prudent. Inactivated vaccines do not interfere with the immune response to other inactivated vaccines or to live vaccines. An inactivated vaccine can be administered either simultaneously or at any time before or after LAIV. Two live vaccines not administered on the same day should be administered ≥ 4 weeks apart when possible.

LAIV and Use of Influenza Antiviral Medications

The effect on safety and efficacy of LAIV coadministration with influenza antiviral medications has not been studied. However, because influenza antivirals reduce replication of influenza viruses, LAIV should not be administered until 48 hours after cessation of influenza antiviral therapy, and influenza antiviral medications should not be administered for 2 weeks after receipt of LAIV.

LAIV Storage

LAIV must be stored at minus 15 degrees C or colder. A manufacturer-supplied freezer box was formerly required for storage of LAIV in a frost-free freezer; however, the freezer box is now optional, and LAIV may now be stored in frost-free freezers without using a freezer box. LAIV can be thawed in a refrigerator and stored at 2 degrees C to 8 degrees C for ≤ 60 hours before use. It should not be refrozen after thawing.

Side Effects and Adverse Reactions

See the "Potential Harms" section in this summary for more information.

Recommended Vaccines for Different Age Groups

When vaccinating children aged 6 months to 3 years, health-care providers should use inactivated influenza vaccine that has been approved by FDA for this age

group. Inactivated influenza vaccine from Sanofi Pasteur, Inc., (FluZone® split-virus) is approved for use among persons aged ≥ 6 months. Inactivated influenza vaccine from Chiron (Fluvirin®) is labeled in the United States for use among persons aged ≥ 4 years because data to demonstrate efficacy among younger persons have not been provided to FDA. Live, attenuated influenza vaccine from MedImmune (FluMist™) is approved for use by healthy persons aged 5 to 49 years (see Table 5 in the original guideline document).

Timing of Annual Influenza Vaccination

The annual supply of influenza vaccine and the timing of its distribution cannot be guaranteed in any year. Information regarding the supply of 2005-2006 vaccine might not be available until late summer or early fall 2005. To allow vaccine providers to plan for the upcoming vaccination season, taking into account the yearly possibility of vaccine delays or shortages and the need to ensure vaccination of persons at high risk and their contacts, ACIP recommends that inactivated influenza vaccine campaigns conducted in October focus primarily on persons at increased risk for influenza complications and their contacts, including health-care workers. Campaigns conducted in November and later should continue to vaccinate persons at high risk and their contacts, but also vaccinate other persons who wish to decrease their risk for influenza infection. Vaccination for all groups should continue into December and beyond. CDC and other public health agencies will assess the vaccine supply on a continuing basis throughout the manufacturing period and will make recommendations preceding the 2005-2006 influenza season regarding the need for tiered timing of inactivated influenza vaccination of different risk groups. Because LAIV is approved for use in healthy persons 5 to 49 years, its use has not been subject to tiered timing.

Vaccination Before October

To avoid missed opportunities for vaccination of persons at high risk for serious complications, such persons should be offered vaccine beginning in September during routine health-care visits or during hospitalizations, if vaccine is available. In facilities housing older persons (e.g., nursing homes), vaccination before October typically should be avoided because antibody levels in such persons can begin to decline within a limited time after vaccination. In addition, children aged < 9 years who have not been previously vaccinated and who need 2 doses before the start of the influenza season can receive their first dose in September so that both doses of the most up-to-date vaccine can be administered before the onset of influenza activity. For previously vaccinated children, 1 dose is needed to provide optimal protection against influenza.

Vaccination in October and November

The optimal time to vaccinate is usually during October through November. ACIP recommends that vaccine providers focus their vaccination efforts in October and earlier primarily on persons aged ≥ 50 years, persons aged < 50 years at increased risk for influenza-related complications (including children aged 6 to 23 months), household contacts of persons at high risk (including out-of-home caregivers and household contacts of children aged 0 to 23 months), and health-care workers. Vaccination of children aged < 9 years who are receiving vaccine for the first time should also begin in October or earlier because those persons need a booster dose

1 month after the initial dose. Efforts to vaccinate other persons who wish to decrease their risk for influenza infection should begin in November; however, if such persons request vaccination in October, vaccination should not be deferred, unless vaccine supplies dictate otherwise. Materials to assist providers in prioritizing early vaccine are available at <http://www.cdc.gov/flu/professionals/vaccination/index.htm> (see also "Travelers" in this report).

Timing of Organized Vaccination Campaigns

Persons and institutions planning substantial organized vaccination campaigns should consider scheduling these events after mid-October because the availability of vaccine in any location cannot be ensured consistently in early fall. Scheduling campaigns after mid-October will minimize the need for cancellations because vaccine is unavailable. Campaigns conducted before November using inactivated vaccine should focus efforts on vaccination of persons aged ≥ 50 years, persons aged < 50 years at increased risk for influenza-related complications (including children aged 6 to 23 months and pregnant women), health-care workers, and household contacts of persons at high-risk (including children aged 0 to 23 months) to the extent feasible. Campaigns using the LAIV are also optimally conducted in October and November.

Vaccination in December and Later

After November, many persons who should or want to receive influenza vaccine remain unvaccinated. In addition, substantial amounts of vaccine are often left over at the end of the influenza season. To improve vaccine coverage, influenza vaccine should continue to be offered in December and throughout the influenza season as long as vaccine supplies are available, even after influenza activity has been documented in the community. In the United States, seasonal influenza activity can begin to increase as early as October or November, but influenza activity has not reached peak levels in the majority of recent seasons until late December to early March (see Table 6 in original guideline document). Therefore, although the timing of influenza activity can vary by region, vaccine administered after November is likely to be beneficial in the majority of influenza seasons. Adults develop peak antibody protection against influenza infection 2 weeks after vaccination.

Strategies for Implementing Vaccination Recommendations in Health-Care Settings

See the "Description of Implementation Strategies" section in this summary for more information.

Recommendations for Using Antiviral Agents for Influenza

Note: Due to increased resistance to adamantanes among influenza A viruses, the antiviral agents amantadine and rimantadine are no longer recommended. Please see the January 2006 addendum at the beginning of the "Major Recommendations" field for further information.

Antiviral drugs for influenza are an adjunct to influenza vaccine for controlling and preventing influenza. However, these agents are not a substitute for vaccination. Four licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir.

Amantadine and rimantadine are chemically related antiviral drugs known as adamantanes with activity against influenza A viruses, but not influenza B viruses. Amantadine was approved in 1966 for chemoprophylaxis of influenza A (H2N2) infection and was later approved in 1976 for treatment and chemoprophylaxis of influenza type A virus infections among adults and children aged ≥ 1 year. Rimantadine was approved in 1993 for treatment and chemoprophylaxis of influenza A infection among adults and prophylaxis among children. Although rimantadine is approved only for chemoprophylaxis of influenza A infection among children, rimantadine treatment for influenza A among children can be beneficial.

Zanamivir and oseltamivir are chemically related antiviral drugs known as neuraminidase inhibitors that have activity against both influenza A and B viruses. Both zanamivir and oseltamivir were approved in 1999 for treating uncomplicated influenza infections. Zanamivir is approved for treating persons aged ≥ 7 years, and oseltamivir is approved for treatment of persons aged ≥ 1 year. In 2000, oseltamivir was approved for chemoprophylaxis of influenza among persons aged ≥ 13 years.

The four drugs differ in pharmacokinetics, side effects, routes of administration, approved age groups, dosages, and costs. An overview of the indications, use, administration, and known primary side effects of these medications is presented in the following sections. Information contained in this report might not represent FDA approval or approved labeling for the antiviral agents described. Package inserts should be consulted for additional information.

Role of Laboratory Diagnosis

Appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. Early diagnosis of influenza can reduce the inappropriate use of antibiotics and provide the option of using antiviral therapy. However, because certain bacterial infections can produce symptoms similar to influenza, bacterial infections should be considered and appropriately treated, if suspected. In addition, bacterial infections can occur as a complication of influenza.

Influenza surveillance information and diagnostic testing can aid clinical judgment and help guide treatment decisions. The accuracy of clinical diagnosis of influenza on the basis of symptoms alone is limited because symptoms from illness caused by other pathogens can overlap considerably with influenza. Influenza surveillance by state and local health departments and CDC can provide information regarding the presence of influenza viruses in the community. Surveillance can also identify the predominant circulating types, influenza A subtypes, and strains of influenza.

Diagnostic tests available for influenza include viral culture, serology, rapid antigen testing, polymerase chain reaction (PCR), and immunofluorescence assays. Sensitivity and specificity of any test for influenza might vary by the laboratory that performs the test, the type of test used, and the type of specimen tested. Among respiratory specimens for viral isolation or rapid detection,

nasopharyngeal specimens are typically more effective than throat swab specimens. As with any diagnostic test, results should be evaluated in the context of other clinical and epidemiologic information available to health-care providers.

Commercial rapid diagnostic tests are available that can detect influenza viruses within 30 minutes. Some tests are approved for use in any outpatient setting, whereas others must be used in a moderately complex clinical laboratory. These rapid tests differ in the types of influenza viruses they can detect and whether they can distinguish between influenza types. Different tests can detect 1) only influenza A viruses; 2) both influenza A and B viruses, but not distinguish between the two types; or 3) both influenza A and B and distinguish between the two.

None of the tests provide any information about influenza A subtypes. The types of specimens acceptable for use (i.e., throat, nasopharyngeal, or nasal aspirates, swabs, or washes) also vary by test. The specificity and, in particular, the sensitivity of rapid tests are lower than for viral culture and vary by test. Because of the lower sensitivity of the rapid tests, physicians should consider confirming negative tests with viral culture or other means because of the possibility of false-negative rapid test results, especially during periods of peak community influenza activity. In contrast, false-positive rapid test results are less likely, but can occur during periods of low influenza activity. Therefore, when interpreting results of a rapid influenza test, physicians should consider the positive and negative predictive values of the test in the context of the level of influenza activity in their community. Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid diagnostic tests. Additional information concerning diagnostic testing is available at <http://www.cdc.gov/flu/professionals/labdiagnosis.htm>.

Despite the availability of rapid diagnostic tests, collecting clinical specimens for viral culture is critical, because only culture isolates can provide specific information regarding circulating strains and subtypes of influenza viruses. This information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions regarding influenza treatment and chemoprophylaxis, and to formulate vaccine for the coming year. Virus isolates also are needed to monitor the emergence of antiviral resistance and the emergence of novel influenza A subtypes that might pose a pandemic threat.

Indications for Use

Treatment

When administered within 2 days of illness onset to otherwise healthy adults, amantadine and rimantadine can reduce the duration of uncomplicated influenza A illness, and zanamivir and oseltamivir can reduce the duration of uncomplicated influenza A and B illness by approximately 1 day, compared with placebo. More clinical data are available concerning the efficacy of zanamivir and oseltamivir for treatment of influenza A infection than for treatment of influenza B infection. However, in vitro data and studies of treatment among mice and ferrets, in addition to clinical studies, have documented that zanamivir and oseltamivir have activity against influenza B viruses.

Data are limited regarding the effectiveness of the four antiviral agents in preventing serious influenza-related complications (e.g., bacterial or viral pneumonia or exacerbation of chronic diseases). Evidence for the effectiveness of these four antiviral drugs is principally based on studies of patients with uncomplicated influenza. Data are limited and inconclusive concerning the effectiveness of amantadine, rimantadine, zanamivir, and oseltamivir for treatment of influenza among persons at high risk for serious complications of influenza. One study assessing oseltamivir treatment primarily among adults reported a reduction in complications, necessitating antibiotic therapy compared with placebo. Fewer studies of the efficacy of influenza antivirals have been conducted among pediatric populations. One study of oseltamivir treatment documented a decreased incidence of otitis media among children. Inadequate data exist regarding the safety and efficacy of any of the influenza antiviral drugs for use among children aged <1 year.

To reduce the emergence of antiviral drug-resistant viruses, amantadine or rimantadine therapy for persons with influenza A illness should be discontinued as soon as clinically warranted, typically after 3 to 5 days of treatment or within 24 to 48 hours after the disappearance of signs and symptoms. The recommended duration of treatment with either zanamivir or oseltamivir is 5 days.

Chemoprophylaxis

Chemoprophylactic drugs are not a substitute for vaccination, although they are critical adjuncts in preventing and controlling influenza. Both amantadine and rimantadine are indicated for chemoprophylaxis of influenza A infection, but not influenza B. Both drugs are approximately 60 to 90 percent effective in preventing illness from influenza A infection. When used as prophylaxis, these antiviral agents can prevent illness while permitting subclinical infection and development of protective antibody against circulating influenza viruses. Therefore, certain persons who take these drugs will develop protective immune responses to circulating influenza viruses. Amantadine and rimantadine do not interfere with the antibody response to the vaccine. Both drugs have been studied extensively among nursing home populations as a component of influenza outbreak-control programs, which can limit the spread of influenza within chronic-care institutions.

Among the neuraminidase inhibitor antivirals zanamivir and oseltamivir, only oseltamivir has been approved for prophylaxis, but community studies of healthy adults indicate that both drugs are similarly effective in preventing febrile, laboratory-confirmed influenza illness (efficacy: zanamivir, 84 percent; oseltamivir, 82 percent). Both antiviral agents have also been reported to prevent influenza illness among persons administered chemoprophylaxis after a household member had influenza diagnosed. Experience with prophylactic use of these agents in institutional settings or among patients with chronic medical conditions is limited in comparison with the adamantanes. One 6-week study of oseltamivir prophylaxis among nursing home residents reported a 92 percent reduction in influenza illness. Use of zanamivir has not been reported to impair the immunologic response to influenza vaccine. Data are not available regarding the efficacy of any of the four antiviral agents in preventing influenza among severely immunocompromised persons.

When determining the timing and duration for administering influenza antiviral medications for prophylaxis, factors related to cost, compliance, and potential side effects should be considered. To be maximally effective as prophylaxis, the drug must be taken each day for the duration of influenza activity in the community. However, to be most cost-effective, one study of amantadine or rimantadine prophylaxis reported that the drugs should be taken only during the period of peak influenza activity in a community.

Persons at High Risk Who Are Vaccinated After Influenza Activity Has Begun: Persons at high risk for complications of influenza still can be vaccinated after an outbreak of influenza has begun in a community. However, development of antibodies in adults after vaccination takes approximately 2 weeks. When influenza vaccine is administered while influenza viruses are circulating, chemoprophylaxis should be considered for persons at high risk during the time from vaccination until immunity has developed. Children aged <9 years who receive influenza vaccine for the first time can require 6 weeks of prophylaxis (i.e., prophylaxis for 4 weeks after the first dose of vaccine and an additional 2 weeks of prophylaxis after the second dose).

Persons Who Provide Care to Those at High Risk: To reduce the spread of virus to persons at high risk during community or institutional outbreaks, chemoprophylaxis during peak influenza activity can be considered for unvaccinated persons who have frequent contact with persons at high risk. Persons with frequent contact include employees of hospitals, clinics, and chronic-care facilities, household members, visiting nurses, and volunteer workers. If an outbreak is caused by a variant strain of influenza that might not be controlled by the vaccine, chemoprophylaxis should be considered for all such persons, regardless of their vaccination status.

Persons Who Have Immune Deficiencies: Chemoprophylaxis can be considered for persons at high risk who are expected to have an inadequate antibody response to influenza vaccine. This category includes persons infected with HIV, chiefly those with advanced HIV disease. No published data are available concerning possible efficacy of chemoprophylaxis among persons with HIV infection or interactions with other drugs used to manage HIV infection. Such patients should be monitored closely if chemoprophylaxis is administered.

Other Persons: Chemoprophylaxis throughout the influenza season or during peak influenza activity might be appropriate for persons at high risk who should not be vaccinated. Chemoprophylaxis can also be offered to persons who wish to avoid influenza illness. Health-care providers and patients should make this decision on an individual basis.

Control of Influenza Outbreaks in Institutions

Using antiviral drugs for treatment and prophylaxis of influenza is a key component of influenza outbreak control in institutions. In addition to antiviral medications, other outbreak-control measures include instituting droplet precautions and establishing cohorts of patients with confirmed or suspected influenza, re-offering influenza vaccinations to unvaccinated staff and patients, restricting staff movement between wards or buildings, and restricting contact between ill staff or visitors and patients (for additional information regarding

outbreak control in specific settings, see "Additional Information Regarding Influenza Infection Control Among Specific Populations" in the original guideline document).

The majority of published reports concerning use of antiviral agents to control influenza outbreaks in institutions are based on studies of influenza A outbreaks among nursing home populations where amantadine or rimantadine were used. Less information is available concerning use of neuraminidase inhibitors in influenza A or B institutional outbreaks. When confirmed or suspected outbreaks of influenza occur in institutions that house persons at high risk, chemoprophylaxis should be started as early as possible to reduce the spread of the virus. In these situations, having preapproved orders from physicians or plans to obtain orders for antiviral medications on short notice can substantially expedite administration of antiviral medications.

When outbreaks occur in institutions, chemoprophylaxis should be administered to all residents, regardless of whether they received influenza vaccinations during the previous fall, and should continue for a minimum of 2 weeks. If surveillance indicates that new cases continue to occur, chemoprophylaxis should be continued until approximately 1 week after the end of the outbreak. The dosage for each resident should be determined individually. Chemoprophylaxis also can be offered to unvaccinated staff who provide care to persons at high risk. Prophylaxis should be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a variant strain of influenza that is not well-matched by the vaccine.

In addition to nursing homes, chemoprophylaxis also can be considered for controlling influenza outbreaks in other closed or semiclosed settings (e.g., dormitories or other settings in which persons live in close proximity). For example, chemoprophylaxis with rimantadine has been used successfully to control an influenza A outbreak aboard a large cruise ship.

To limit the potential transmission of drug-resistant virus during outbreaks in institutions, whether in chronic or acute-care settings or other closed settings, measures should be taken to reduce contact as much as possible between persons taking antiviral drugs for treatment and other persons, including those taking chemoprophylaxis (see "Antiviral Drug-Resistant Strains of Influenza" in the original guideline document).

Dosage

Dosage recommendations vary by age group and medical conditions (see Table 7 in the original guideline document).

Children

Amantadine: Use of amantadine among children aged <1 year has not been adequately evaluated. The FDA-approved dosage for children aged 1 to 9 years for treatment and prophylaxis is 4.4 to 8.8 mg/kg body weight/day, not to exceed 150 mg/day. Although further studies are needed to determine the optimal dosage for children aged 1 to 9 years, physicians should consider prescribing only 5 mg/kg body weight/day (not to exceed 150 mg/day) to reduce the risk for

toxicity. The approved dosage for children aged ≥ 10 years is 200 mg/day (100 mg twice a day); however, for children weighing < 40 kg, prescribing 5 mg/kg body weight/day, regardless of age, is advisable.

Rimantadine: Rimantadine is approved for prophylaxis among children aged ≥ 1 year and for treatment and prophylaxis among adults. Although rimantadine is approved only for prophylaxis of infection among children, certain specialists in the management of influenza consider it appropriate for treatment among children. Use of rimantadine among children aged < 1 year has not been adequately evaluated. Rimantadine should be administered in 1 or 2 divided doses at a dosage of 5 mg/kg body weight/day, not to exceed 150 mg/day for children aged 1 to 9 years. The approved dosage for children aged ≥ 10 years is 200 mg/day (100 mg twice a day); however, for children weighing < 40 kg, prescribing 5 mg/kg body weight/day, regardless of age, is recommended.

Zanamivir: Zanamivir is approved for treatment among children aged ≥ 7 years. The recommended dosage of zanamivir for treatment of influenza is two inhalations (one 5-mg blister per inhalation for a total dose of 10 mg) twice daily (approximately 12 hours apart).

Oseltamivir: Oseltamivir is approved for treatment among persons aged ≥ 1 year and for chemoprophylaxis among persons aged ≥ 13 years. Recommended treatment dosages for children vary by the weight of the child: the dosage recommendation for children who weigh ≤ 15 kg is 30 mg twice a day; for children weighing > 15 to 23 kg, the dosage is 45 mg twice a day; for those weighing > 23 to 40 kg, the dosage is 60 mg twice a day; and for children weighing > 40 kg, the dosage is 75 mg twice a day. The treatment dosage for persons aged ≥ 13 years is 75 mg twice daily. For children aged ≥ 13 years, the recommended dose for prophylaxis is 75 mg once a day.

Persons Aged > 65 Years

Amantadine: The daily dosage of amantadine for persons aged ≥ 65 years should not exceed 100 mg for prophylaxis or treatment, because renal function declines with increasing age. For certain older persons, the dose should be further reduced.

Rimantadine: Among older persons, the incidence and severity of central nervous system (CNS) side effects are substantially lower among those taking rimantadine at a dosage of 100 mg/day than among those taking amantadine at dosages adjusted for estimated renal clearance. However, chronically ill older persons have had a higher incidence of CNS and gastrointestinal symptoms and serum concentrations 2 to 4 times higher than among healthy, younger persons when rimantadine has been administered at a dosage of 200 mg/day.

For prophylaxis among persons aged ≥ 65 years, the recommended dosage is 100 mg/day. For treatment of older persons in the community, a reduction in dosage to 100 mg/day should be considered if they experience side effects when taking a dosage of 200 mg/day. For treatment of older nursing home residents, the dosage of rimantadine should be reduced to 100 mg/day.

Zanamivir and Oseltamivir: No reduction in dosage is recommended on the basis of age alone.

Persons with Impaired Renal Function

Amantadine: A reduction in dosage is recommended for patients with creatinine clearance ≤ 50 mL/min. Guidelines for amantadine dosage on the basis of creatinine clearance are located in the package insert. Because recommended dosages on the basis of creatinine clearance might provide only an approximation of the optimal dose for a given patient, such persons should be observed carefully for adverse reactions. If necessary, further reduction in the dose or discontinuation of the drug might be indicated because of side effects. Hemodialysis contributes minimally to amantadine clearance.

Rimantadine: A reduction in dosage to 100 mg/day is recommended for persons with creatinine clearance < 10 mL/min. Because of the potential for accumulation of rimantadine and its metabolites, patients with any degree of renal insufficiency, including older persons, should be monitored for adverse effects, and either the dosage should be reduced or the drug should be discontinued, if necessary. Hemodialysis contributes minimally to drug clearance.

Zanamivir: Limited data are available regarding the safety and efficacy of zanamivir for patients with impaired renal function. Among patients with renal failure who were administered a single intravenous dose of zanamivir, decreases in renal clearance, increases in half-life, and increased systemic exposure to zanamivir were observed. However, a limited number of healthy volunteers who were administered high doses of intravenous zanamivir tolerated systemic levels of zanamivir that were substantially higher than those resulting from administration of zanamivir by oral inhalation at the recommended dose. On the basis of these considerations, the manufacturer recommends no dose adjustment for inhaled zanamivir for a 5-day course of treatment for patients with either mild-to-moderate or severe impairment in renal function.

Oseltamivir: Serum concentrations of oseltamivir carboxylate (GS4071), the active metabolite of oseltamivir, increase with declining renal function. For patients with creatinine clearance of 10 to 30 mL/min, a reduction of the treatment dosage of oseltamivir to 75 mg once daily and in the prophylaxis dosage to 75 mg every other day is recommended. No treatment or prophylaxis dosing recommendations are available for patients undergoing routine renal dialysis treatment.

Persons with Liver Disease

Amantadine: No increase in adverse reactions to amantadine has been observed among persons with liver disease. Rare instances of reversible elevation of liver enzymes among patients receiving amantadine have been reported, although a specific relation between the drug and such changes has not been established.

Rimantadine: A reduction in dosage to 100 mg/day is recommended for persons with severe hepatic dysfunction.

Zanamivir and Oseltamivir: Neither of these medications has been studied among persons with hepatic dysfunction.

Persons with Seizure Disorders

Amantadine: An increased incidence of seizures has been reported among patients with a history of seizure disorders who have received amantadine. Patients with seizure disorders should be observed closely for possible increased seizure activity when taking amantadine.

Rimantadine: Seizures (or seizure-like activity) have been reported among persons with a history of seizures who were not receiving anticonvulsant medication while taking rimantadine. The extent to which rimantadine might increase the incidence of seizures among persons with seizure disorders has not been adequately evaluated.

Zanamivir and Oseltamivir: Seizure events have been reported during postmarketing use of zanamivir and oseltamivir, although no epidemiologic studies have reported any increased risk for seizures with either zanamivir or oseltamivir use.

Route

Amantadine, rimantadine, and oseltamivir are administered orally. Amantadine and rimantadine are available in tablet or syrup form, and oseltamivir is available in capsule or oral suspension form. Zanamivir is available as a dry powder that is self-administered via oral inhalation by using a plastic device included in the package with the medication. Patients will benefit from instruction and demonstration of correct use of this device.

Side Effects and Adverse Reactions

See the "Potential Harms" section of this summary for more information.

Use During Pregnancy

No clinical studies have been conducted regarding the safety or efficacy of amantadine, rimantadine, zanamivir, or oseltamivir for pregnant women; only two cases of amantadine use for severe influenza illness during the third trimester have been reported. However, both amantadine and rimantadine have been demonstrated in animal studies to be teratogenic and embryotoxic when administered at substantially high doses. Because of the unknown effects of influenza antiviral drugs on pregnant women and their fetuses, these four drugs should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus (see manufacturers' package inserts).

Drug Interactions

Careful observation is advised when amantadine is administered concurrently with drugs that affect CNS, including CNS stimulants. Concomitant administration of antihistamines or anticholinergic drugs can increase the incidence of adverse CNS

reactions. No clinically substantial interactions between rimantadine and other drugs have been identified.

Clinical data are limited regarding drug interactions with zanamivir. However, no known drug interactions have been reported, and no clinically critical drug interactions have been predicted on the basis of in vitro data and data from studies using rats.

Limited clinical data are available regarding drug interactions with oseltamivir. Because oseltamivir and oseltamivir carboxylate are excreted in the urine by glomerular filtration and tubular secretion via the anionic pathway, a potential exists for interaction with other agents excreted by this pathway. For example, coadministration of oseltamivir and probenecid resulted in reduced clearance of oseltamivir carboxylate by approximately 50 percent and a corresponding approximate twofold increase in the plasma levels of oseltamivir carboxylate.

No published data are available concerning the safety or efficacy of using combinations of any of these four influenza antiviral drugs. For more detailed information concerning potential drug interactions for any of these influenza antiviral drugs, package inserts should be consulted.

Antiviral Drug-Resistant Strains of Influenza

Amantadine-resistant viruses are cross-resistant to rimantadine and vice versa. Drug-resistant viruses can appear in approximately one third of patients when either amantadine or rimantadine is used for therapy. During the course of amantadine or rimantadine therapy, resistant influenza strains can replace susceptible strains within 2 to 3 days of starting therapy. Resistant viruses have been isolated from persons who live at home or in an institution where other residents are taking or have recently taken amantadine or rimantadine as therapy; however, the frequency with which resistant viruses are transmitted and their effect on efforts to control influenza are unknown. Amantadine- and rimantadine-resistant viruses are not more virulent or transmissible than susceptible viruses. The screening of epidemic strains of influenza A has rarely detected amantadine- and rimantadine-resistant viruses.

Persons who have influenza A infection and who are treated with either amantadine or rimantadine can shed susceptible viruses early in the course of treatment and later shed drug-resistant viruses, including after 5 to 7 days of therapy. Such persons can benefit from therapy even when resistant viruses emerge.

Resistance to zanamivir and oseltamivir can be induced in influenza A and B viruses in vitro, but induction of resistance usually requires multiple passages in cell culture. By contrast, resistance to amantadine and rimantadine in vitro can be induced with fewer passages in cell culture. Development of viral resistance to zanamivir and oseltamivir during treatment has been identified but does not appear to be frequent. In one pediatric study, 5.5 percent of patients treated with oseltamivir had posttreatment isolates that were resistant to neuraminidase inhibitors. One limited study of Japanese children treated with oseltamivir reported a high frequency of resistant viruses. However, no transmission of neuraminidase inhibitor resistant viruses in humans has been documented to

date. No isolates with reduced susceptibility to zanamivir have been reported from clinical trials, although the number of posttreatment isolates tested is limited, and the risk for emergence of zanamivir-resistant isolates cannot be quantified. Only one clinical isolate with reduced susceptibility to zanamivir, obtained from an immunocompromised child on prolonged therapy, has been reported. Available diagnostic tests are not optimal for detecting clinical resistance to the neuraminidase inhibitor antiviral drugs, and additional tests are being developed. Postmarketing surveillance for neuraminidase inhibitor-resistant influenza viruses is being conducted.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Potential Benefits of Vaccination

- Vaccination is associated with reductions in influenza-related respiratory illness and physician visits among all age groups, hospitalization and death among persons at high risk, otitis media among children, and work absenteeism among adults.
- When vaccine and epidemic strains are well-matched, achieving increased vaccination rates among persons living in closed settings (e.g., nursing homes and other chronic-care facilities) and among staff can reduce the risk for outbreaks by inducing herd immunity. Vaccination of health-care workers and other persons in close contact with persons at increased risk for severe influenza illness can also reduce transmission of influenza and subsequent influenza-related complications.

Efficacy and Effectiveness of Inactivated Influenza Vaccine

The effectiveness of inactivated influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation. The majority of vaccinated children and young adults develop high postvaccination hemagglutination inhibition antibody titers. These antibody titers are protective against illness caused by strains that are antigenically similar to those strains of the same type or subtype included in the vaccine.

Adults Aged <65 Years. When the vaccine and circulating viruses are antigenically similar, influenza vaccine prevents influenza illness among approximately 70 to 90 percent of healthy adults aged <65 years. Vaccination of healthy adults also has resulted in decreased work absenteeism and decreased use of health-care resources, including use of antibiotics, when the vaccine and circulating viruses are well-matched. In a case-control study of adults aged 50 to 64 years with laboratory-confirmed influenza during the 2003-2004 season when the vaccine and circulating viruses were not well matched, vaccine effectiveness was estimated to be 52 percent among healthy persons and 38 percent among those with one or more high-risk conditions.

Children. Children aged ≥ 6 months can develop protective levels of anti-influenza antibody against specific influenza virus strains after influenza vaccination, although the antibody response among children at high risk for influenza-related complications might be lower than among healthy children. In a randomized study among children aged 1 to 15 years, inactivated influenza vaccine was 77 to 91 percent effective against influenza respiratory illness and was 44 to 49 percent, 74 to 76 percent, and 70 to 81 percent effective against influenza seroconversion among children aged 1 to 5, 6 to 10, and 11 to 15 years, respectively. One study reported a vaccine efficacy of 56 percent against influenza illness among healthy children aged 3 to 9 years, and another study determined vaccine efficacy of 22 to 54 percent and 60 to 78 percent among children with asthma aged 2 to 6 years and 7 to 14 years, respectively. A 2-year randomized study of children aged 6 to 24 months determined that ≥ 89 percent of children seroconverted to all three vaccine strains during both years. During year 1, among 411 children, vaccine efficacy was 66 percent (95 percent confidence interval [CI] = 34 to 82 percent) against culture-confirmed influenza (attack rates: 5.5 percent and 15.9 percent among vaccine and placebo groups, respectively). During year 2, among 375 children, vaccine efficacy was -7 percent (95 percent CI = -247 to 67 percent; attack rates: 3.6 percent and 3.3 percent among vaccine and placebo groups, respectively; the second year exhibited lower attack rates overall and was considered a mild season). However, no overall reduction in otitis media was reported. Other studies report that trivalent inactivated influenza vaccine decreases the incidence of influenza-associated otitis media among young children by approximately 30 percent. A retrospective study among approximately 5,000 children aged 6 to 23 months conducted during a year with a suboptimal vaccine match indicated vaccine effectiveness of 49 percent against medically attended, clinically diagnosed pneumonia or influenza among children who had received 2 doses of influenza vaccine. No effectiveness was demonstrated among children who had received only 1 dose of influenza vaccine, illustrating the importance of administering 2 doses of vaccine to previously unvaccinated children aged <9 years.

Adults Aged ≥ 65 Years. Older persons and persons with certain chronic diseases might develop lower postvaccination antibody titers than healthy young adults and thus can remain susceptible to influenza infection and influenza-related upper respiratory tract illness. A randomized trial among noninstitutionalized persons aged ≥ 60 years reported a vaccine efficacy of 58 percent against influenza respiratory illness, but indicated that efficacy might be lower among those aged ≥ 70 years. The vaccine can also be effective in preventing secondary complications and reducing the risk for influenza-related hospitalization and death among adults aged ≥ 65 years with and without high-risk medical conditions (e.g.,

heart disease and diabetes). Among elderly persons not living in nursing homes or similar chronic-care facilities, influenza vaccine is 30 to 70 percent effective in preventing hospitalization for pneumonia and influenza. Among older persons who do reside in nursing homes, influenza vaccine is most effective in preventing severe illness, secondary complications, and deaths. Among this population, the vaccine can be 50 to 60 percent effective in preventing influenza-related hospitalization or pneumonia and 80 percent effective in preventing influenza-related death, although the effectiveness in preventing influenza illness often ranges from 30 to 40 percent.

Efficacy and Effectiveness of Live Attenuated Influenza Vaccine (LAIV)

Healthy Children. A randomized, double-blind, placebo-controlled trial among 1,602 healthy children initially aged 15 to 71 months assessed the efficacy of trivalent LAIV against culture-confirmed influenza during two seasons. This trial included subsets of 238 healthy children (163 vaccinees and 75 placebo recipients) aged 60 to 71 months who received 2 doses and 74 children (54 vaccinees and 20 placebo recipients) aged 60 to 71 months who received a single dose during season one, and a subset of 544 children (375 vaccinees and 169 placebo recipients) aged 60 to 84 months during season two. Children who continued in the study remained in the same study group. In season one, when vaccine and circulating virus strains were well-matched, efficacy was 93 percent for all participants, regardless of age, among persons receiving 2 doses of LAIV. Efficacy was 87 percent in the 60 to 71 month subset for those who received 2 doses, and was 91 percent in the subset for those who received 1 or 2 doses. In season two, when the A (H3N2) component was not well-matched between vaccine and circulating virus strains, efficacy was 86 percent overall and 87 percent among those aged 60 to 84 months. The vaccine was 92 percent efficacious in preventing culture-confirmed influenza during the two-season study. Other results included a 27 percent reduction in febrile otitis media and a 28 percent reduction in otitis media with concomitant antibiotic use. Receipt of LAIV also resulted in a 30 percent lower incidence of febrile otitis media and 21 percent fewer febrile illnesses. Another study assessing LAIV effectiveness in children aged 18 months to 18 years indicated effectiveness against medically attended acute respiratory illness (MAARI) of 18 percent. However, applying a validation sample of surveillance cultures with MAARI demonstrated efficacy of 92 percent against influenza A (H1N1) and 66 percent against an influenza B drift variant.

Healthy Adults. A randomized, double-blind, placebo-controlled trial among 4,561 healthy working adults aged 18 to 64 years assessed multiple endpoints, including reductions in illness, absenteeism, health-care visits, and medication use during peak and total influenza outbreak periods. The study was conducted during the 1997-1998 influenza season, when the vaccine and circulating A (H3N2) strains were not well-matched. The study did not include testing of viruses by a laboratory. During peak outbreak periods, no difference was identified between LAIV and placebo recipients experiencing any febrile episodes. However, vaccination was associated with reductions in severe febrile illnesses of 19 percent and febrile upper respiratory tract illnesses of 24 percent. Vaccination also was associated with fewer days of illness, fewer days of work lost, fewer days with health-care-provider visits, and reduced use of prescription antibiotics and over-the-counter medications.

Among the subset of 3,637 healthy adults aged 18 to 49 years, LAIV recipients (n = 2,411) had 26 percent fewer febrile upper-respiratory illness episodes; 27 percent fewer lost work days as a result of febrile upper respiratory illness; and 18 to 37 percent fewer days of health-care provider visits caused by febrile illness, compared with placebo recipients (n = 1,226). Days of antibiotic use were reduced by 41 to 45 percent in this age subset.

Another randomized, double-blind, placebo-controlled challenge study among 92 healthy adults (LAIV, n = 29; placebo, n = 31; inactivated influenza vaccine, n = 32) aged 18 to 41 years assessed the efficacy of both LAIV and inactivated vaccine. The overall efficacy of LAIV and inactivated influenza vaccine in preventing laboratory-documented influenza from all three influenza strains combined was 85 percent and 71 percent, respectively, on the basis of experimental challenge by viruses to which study participants were susceptible before vaccination. The difference in efficacy between the two vaccines was not statistically significant.

POTENTIAL HARMS

Inactivated Influenza Vaccine

Side Effects and Adverse Reactions

When educating patients regarding potential side effects, clinicians should emphasize that 1) inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza; and 2) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination.

Local Reactions

In placebo-controlled studies among adults, the most frequent side effect of vaccination is soreness at the vaccination site (affecting 10 to 64 percent of patients) that lasts <2 days. These local reactions typically are mild and rarely interfere with the person's ability to conduct usual daily activities. One blinded, randomized, cross-over study among 1,952 adults and children with asthma, demonstrated that only body aches were reported more frequently after inactivated influenza vaccine (25.1 percent) than placebo-injection (20.8 percent). One study reported 20 to 28 percent of children with asthma aged 9 months to 18 years with local pain and swelling, and another study reported 23 percent of children aged 6 months to 4 years with chronic heart or lung disease had local reactions. A different study reported no difference in local reactions among 53 children aged 6 months to 6 years with high-risk medical conditions or among 305 healthy children aged 3 to 12 years in a placebo-controlled trial of inactivated influenza vaccine. In a study of 12 children aged 5 to 32 months, no substantial local or systemic reactions were noted.

Systemic Reactions

Fever, malaise, myalgia, and other systemic symptoms can occur after vaccination with inactivated vaccine and most often affect persons who have had no previous exposure to the influenza virus antigens in the vaccine (e.g., young children).

These reactions begin 6 to 12 hours after vaccination and can persist for 1 to 2 days. Recent placebo-controlled trials demonstrate that among older persons and healthy young adults, administration of split-virus influenza vaccine is not associated with higher rates of systemic symptoms (e.g., fever, malaise, myalgia, and headache) when compared with placebo injections.

Less information from published studies is available for children, compared with adults. However, in a randomized cross-over study among both children and adults with asthma, no increase in asthma exacerbations was reported for either age group. An analysis of 215,600 children aged <18 years and 8,476 children aged 6 to 23 months enrolled in one of five health maintenance organizations reported no increase in biologically plausible medically attended events during the 2 weeks after inactivated influenza vaccination, compared with control periods 3 to 4 weeks before and after vaccination. In a study of 791 healthy children, post-vaccination fever was noted among 11.5 percent of children aged 1 to 5 years, 4.6 percent among children aged 6 to 10 years, and 5.1 percent among children aged 11 to 15 years. Among children with high-risk medical conditions, one study of 52 children aged 6 months to 4 years reported fever among 27 percent and irritability and insomnia among 25 percent; and a study among 33 children aged 6 to 18 months reported that one child had irritability and one had a fever and seizure after vaccination. No placebo comparison was made in these studies. However, in pediatric trials of A/New Jersey/76 swine influenza vaccine, no difference was reported between placebo and split-virus vaccine groups in febrile reactions after injection, although the vaccine was associated with mild local tenderness or erythema.

Limited data regarding potential adverse events after influenza vaccination are available from the Vaccine Adverse Event Reporting System (VAERS). During January 1, 1991 to June 30, 2004, VAERS received 1,895 reports of adverse events among children aged <18 years, including 479 reports of adverse events among children aged 6 to 23 months. The number of influenza vaccine doses received by children during this entire period is unknown (Centers for Disease Control and Prevention (CDC), unpublished data, 2005). A recently published review of VAERS reports of trivalent inactivated influenza vaccine (TIV) in children aged 6 to 23 months documented that the most frequently reported adverse events were fever, rash, injection-site reactions, and seizures. The majority of the small total number of reported seizures appeared to be febrile. Because of the limitations of passive reporting systems, determining causality for specific types of adverse events, with the exception of injection-site reactions, is usually not possible by using VAERS data alone. A population-based study of TIV safety in children aged 6 to 23 months indicated no vaccine associated adverse events that had a plausible relationship to vaccination.

Health-care professionals should promptly report to VAERS all clinically significant adverse events after influenza vaccination of children, even if the health-care professional is not certain that the vaccine caused the event. The Institute of Medicine has specifically recommended reporting of potential neurologic complications (e.g., demyelinating disorders such as Guillain-Barré syndrome [GBS]), although no evidence exists of a causal relationship between influenza vaccine and neurologic disorders in children.

Immediate, presumably allergic, reactions (e.g., hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to certain vaccine components; the majority of reactions probably are caused by residual egg protein. Although current influenza vaccines contain only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have had hives or swelling of the lips or tongue, or who have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons who have documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein, might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered. Protocols have been published for safely administering influenza vaccine to persons with egg allergies.

Hypersensitivity reactions to any vaccine component can occur. Although exposure to vaccines containing thimerosal can lead to induction of hypersensitivity, the majority of patients do not have reactions to thimerosal when it is administered as a component of vaccines, even when patch or intradermal tests for thimerosal indicate hypersensitivity. When reported, hypersensitivity to thimerosal usually has consisted of local, delayed hypersensitivity reactions.

Guillain-Barré Syndrome

The 1976 swine influenza vaccine was associated with an increased frequency of GBS. Among persons who received the swine influenza vaccine in 1976, the rate of GBS was <10 cases/1 million persons vaccinated. The risk for influenza vaccine-associated GBS is higher among persons aged ≥ 25 years than persons <25 years. Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. Obtaining strong epidemiologic evidence for a possible limited increase in risk is difficult for such a rare condition as GBS, which has an annual incidence of 10-20 cases/1 million adults. More definitive data probably will require using other methodologies (e.g., laboratory studies of the pathophysiology of GBS).

During three of four influenza seasons studied during 1977 to 1991, the overall relative risk estimates for GBS after influenza vaccination were slightly elevated but were not statistically significant in any of these studies. However, in a study of the 1992-1993 and 1993-1994 seasons, the overall relative risk for GBS was 1.7 (95 percent CI = 1.0 to 2.8; $p = 0.04$) during the 6 weeks after vaccination, representing approximately 1 additional case of GBS/1 million persons vaccinated. The combined number of GBS cases peaked 2 weeks after vaccination. Thus, investigations to date have not documented a substantial increase in GBS associated with influenza vaccines (other than the swine influenza vaccine in 1976), and that, if influenza vaccine does pose a risk, it is probably slightly more than one additional case/1 million persons vaccinated. Recent data from VAERS has documented decreased reporting of post influenza vaccine GBS across age groups, despite overall increased reporting for influenza vaccine. Cases of GBS after influenza infection have been reported, but no epidemiologic studies have documented such an association. Substantial evidence exists that multiple

infectious illnesses, most notably *Campylobacter jejuni*, and upper respiratory tract infections are associated with GBS.

Even if GBS were a true side effect of vaccination in the years after 1976, the estimated risk for GBS of approximately 1 additional case/1 million persons vaccinated is substantially less than the risk for severe influenza, which can be prevented by vaccination among all age groups, especially persons aged ≥ 65 years and those who have medical indications for influenza vaccination (see Table 1 and "Hospitalizations and Deaths from Influenza" in the original guideline document). The potential benefits of influenza vaccination in preventing serious illness, hospitalization, and death substantially outweigh the possible risks for experiencing vaccine-associated GBS. The average case fatality ratio for GBS is 6 percent and increases with age. No evidence indicates that the case fatality ratio for GBS differs among vaccinated persons and those not vaccinated.

The incidence of GBS among the general population is low, but persons with a history of GBS have a substantially greater likelihood of subsequently experiencing GBS than persons without such a history. Thus, the likelihood of coincidentally experiencing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is unknown; therefore, avoiding vaccinating persons who are not at high risk for severe influenza complications and who are known to have experienced GBS within 6 weeks after a previous influenza vaccination is prudent. As an alternative, physicians might consider using influenza antiviral chemoprophylaxis for these persons. Although data are limited, for the majority of persons who have a history of GBS and who are at high risk for severe complications from influenza, the established benefits of influenza vaccination justify yearly vaccination.

Live Attenuated Influenza Vaccine (LAIV)

Side Effects and Adverse Reactions

Twenty prelicensure clinical trials assessed the safety of the approved LAIV. In these combined studies, approximately 28,000 doses of the vaccine were administered to approximately 20,000 subjects. A subset of these trials were randomized, placebo-controlled studies in which an estimated 4,000 healthy children aged 5 to 17 years and 2,000 healthy adults aged 18 to 49 years were vaccinated. The incidence of adverse events possibly complicating influenza (e.g., pneumonia, bronchitis, bronchiolitis, or central nervous system events) was not statistically different among LAIV and placebo recipients aged 5 to 49 years. LAIV is made from attenuated viruses and does not cause influenza in vaccine recipients.

Children. In a subset of healthy children aged 60 to 71 months from one clinical trial, certain signs and symptoms were reported more often among LAIV recipients after the first dose ($n = 214$) than placebo recipients ($n = 95$) (e.g., runny nose, 48.1 percent versus 44.2 percent; headache, 17.8 percent versus 11.6 percent; vomiting, 4.7 percent versus 3.2 percent; and myalgias, 6.1 percent versus 4.2 percent), but these differences were not statistically significant. In other trials, signs and symptoms reported after LAIV administration

have included runny nose or nasal congestion (20 to 75 percent), headache (2 to 46 percent), fever (0 to 26 percent), vomiting (3 to 13 percent), abdominal pain (2 percent), and myalgias (0 to 21 percent). These symptoms were associated more often with the first dose and were self-limited. Unpublished data from a study including subjects aged 1 to 17 years indicated an increase in asthma or reactive airways disease in the subset aged 12 to 59 months. Because of this, LAIV is not approved for use among children aged <60 months.

Adults. Among adults, runny nose or nasal congestion (28 to 78 percent), headache (16 to 44 percent), and sore throat (15 to 27 percent) have been reported more often among vaccine recipients than placebo recipients. In one clinical trial among a subset of healthy adults aged 18 to 49 years, signs and symptoms reported more frequently among LAIV recipients (n = 2,548) than placebo recipients (n = 1,290) within 7 days after each dose included cough (13.9 percent versus 10.8 percent); runny nose (44.5 percent versus 27.1 percent); sore throat (27.8 percent versus 17.1 percent); chills (8.6 percent versus 6.0 percent); and tiredness/weakness (25.7 percent versus 21.6 percent).

Safety Among Groups at High Risk from Influenza-Related Morbidity. Until additional data are acquired and analyzed, persons at high risk for experiencing complications from influenza infection (e.g., immunocompromised patients; patients with asthma, cystic fibrosis, or chronic obstructive pulmonary disease; or persons aged ≥ 65 years) should not be vaccinated with LAIV. Protection from influenza among these groups should be accomplished by using inactivated influenza vaccine.

Serious Adverse Events. Serious adverse events among healthy children aged 5 to 17 years or healthy adults aged 18 to 49 years occurred at a rate of <1 percent. Surveillance should continue for adverse events that might not have been detected in previous studies. A preliminary review of reports to VAERS after distribution of approximately 800,000 doses during the 2003-2004 influenza season did not reveal any substantial new safety concerns. Health-care professionals should promptly report all clinically significant adverse events after LAIV administration to VAERS, as recommended for inactivated influenza vaccine.

Influenza Antiviral Medications

Side Effects and Adverse Reactions

When considering use of influenza antiviral medications (i.e., choice of antiviral drug, dosage, and duration of therapy), clinicians must consider the patient's age, weight, and renal function (see Table 7 in the original guideline document); presence of other medical conditions; indications for use (i.e., prophylaxis or therapy); and the potential for interaction with other medications.

Amantadine and Rimantadine

Note: Due to increased resistance to adamantanes among influenza A viruses, the antiviral agents amantadine and rimantadine are no longer recommended. Please see the January 2006 addendum at the beginning of the "Major Recommendations" field for further information.

Both amantadine and rimantadine can cause central nervous system (CNS) and gastrointestinal side effects when administered to young, healthy adults at equivalent dosages of 200 mg/day. However, incidence of CNS side effects (e.g., nervousness, anxiety, insomnia, difficulty concentrating, and lightheadedness) is higher among persons taking amantadine than among those taking rimantadine. In a 6-week study of prophylaxis among healthy adults, approximately 6 percent of participants taking rimantadine at a dosage of 200 mg/day experienced one or more CNS symptoms, compared with approximately 13 percent of those taking the same dosage of amantadine and 4 percent of those taking placebo. A study of older persons also demonstrated fewer CNS side effects associated with rimantadine compared with amantadine. Gastrointestinal side effects (e.g., nausea and anorexia) occur among approximately 1 to 3 percent of persons taking either drug, compared with 1 percent of persons receiving the placebo.

Side effects associated with amantadine and rimantadine are usually mild and cease soon after discontinuing the drug. Side effects can diminish or disappear after the first week, despite continued drug ingestion. However, serious side effects have been observed (e.g., marked behavioral changes, delirium, hallucinations, agitation, and seizures). These more severe side effects have been associated with high plasma drug concentrations and have been observed most often among persons who have renal insufficiency, seizure disorders, or certain psychiatric disorders and among older persons who have been taking amantadine as prophylaxis at a dosage of 200 mg/day. Clinical observations and studies have indicated that lowering the dosage of amantadine among these persons reduces the incidence and severity of such side effects (see Table 7 in the original guideline document). In acute overdosage of amantadine, CNS, renal, respiratory, and cardiac toxicity, including arrhythmias, have been reported. Because rimantadine has been marketed for a shorter period than amantadine, its safety among certain patient populations (e.g., chronically ill and older persons) has been evaluated less frequently. Because amantadine has anticholinergic effects and might cause mydriasis, it should not be used among patients with untreated angle closure glaucoma.

Zanamivir

In a study of zanamivir treatment of influenza-like illness (ILI) among persons with asthma or chronic obstructive pulmonary disease where study medication was administered after use of a Beta₂-agonist, 13 percent of patients receiving zanamivir and 14 percent of patients who received placebo (inhaled powdered lactose vehicle) experienced a >20 percent decline in forced expiratory volume in 1 second (FEV₁) after treatment. However, in a phase-I study of persons with mild or moderate asthma who did not have ILI, one of 13 patients experienced bronchospasm after administration of zanamivir. In addition, during postmarketing surveillance, cases of respiratory function deterioration after inhalation of zanamivir have been reported. Certain patients had underlying airway disease (e.g., asthma or chronic obstructive pulmonary disease). Because of the risk for serious adverse events and because the efficacy has not been demonstrated among this population, zanamivir is not recommended for treatment for patients with underlying airway disease. If physicians decide to prescribe zanamivir to patients with underlying chronic respiratory disease after carefully considering potential risks and benefits, the drug should be used with caution under conditions of appropriate monitoring and supportive care, including

the availability of short-acting bronchodilators. Patients with asthma or chronic obstructive pulmonary disease who use zanamivir are advised to 1) have a fast-acting inhaled bronchodilator available when inhaling zanamivir and 2) stop using zanamivir and contact their physician if they experience difficulty breathing. No definitive evidence is available regarding the safety or efficacy of zanamivir for persons with underlying respiratory or cardiac disease or for persons with complications of acute influenza. Allergic reactions, including oropharyngeal or facial edema, have also been reported during postmarketing surveillance.

In clinical treatment studies of persons with uncomplicated influenza, the frequencies of adverse events were similar for persons receiving inhaled zanamivir and for those receiving placebo (i.e., inhaled lactose vehicle alone). The most common adverse events reported by both groups were diarrhea; nausea; sinusitis; nasal signs and symptoms; bronchitis; cough; headache; dizziness; and ear, nose, and throat infections. Each of these symptoms was reported by <5 percent of persons in the clinical treatment studies combined.

Oseltamivir

Nausea and vomiting were reported more frequently among adults receiving oseltamivir for treatment (nausea without vomiting, approximately 10 percent; vomiting, approximately 9 percent) than among persons receiving placebo (nausea without vomiting, approximately 6 percent; vomiting, approximately 3 percent). Among children treated with oseltamivir, 14.3 percent had vomiting, compared with 8.5 percent of placebo recipients. Overall, 1 percent discontinued the drug secondary to this side effect, whereas a limited number of adults who were enrolled in clinical treatment trials of oseltamivir discontinued treatment because of these symptoms. Similar types and rates of adverse events were reported in studies of oseltamivir prophylaxis. Nausea and vomiting might be less severe if oseltamivir is taken with food.

CONTRAINDICATIONS

CONTRAINDICATIONS

Inactivated Influenza Vaccine

Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine without first consulting a physician (see "Potential Harms" section in this summary). Prophylactic use of antiviral agents is an option for preventing influenza among such persons. However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at high risk for complications from influenza can benefit from vaccine after appropriate allergy evaluation and desensitization. Information regarding vaccine components is located in package inserts from each manufacturer. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. However, minor illnesses with or without fever do not contraindicate use of influenza vaccine, particularly among children with mild upper-respiratory-tract infection or allergic rhinitis.

Live Attenuated Influenza Vaccine (LAIV)

The following populations should not be vaccinated with LAIV:

- Persons aged <5 years or those aged ≥ 50 years*
- Persons with asthma, reactive airways disease, or other chronic disorders of the pulmonary or cardiovascular systems; persons with other underlying medical conditions, including such metabolic diseases as diabetes, renal dysfunction, and hemoglobinopathies; or persons with known or suspected immunodeficiency diseases or who are receiving immunosuppressive therapies*
- Children or adolescents receiving aspirin or other salicylates (because of the association of Reye syndrome with wild-type influenza infection)*
- Persons with a history of GBS
- Pregnant women*
- Persons with a history of hypersensitivity, including anaphylaxis, to any of the components of LAIV or to eggs

* These persons should receive inactivated influenza vaccine.

QUALIFYING STATEMENTS

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- Information contained in this report might not represent U.S. Food and Drug Administration (FDA) approval or approved labeling for the antiviral agents described. Package inserts should be consulted for additional information.
- Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

January 2006 Addendum

On January 14, 2006, a Centers for Disease Control and Prevention (CDC) Health Alert (available at <http://www.cdc.gov/flu/han011406.htm>) with interim recommendations against the use of amantadine and rimantadine for the treatment or prophylaxis of influenza in the United States during the 2005-06 influenza season was sent via the Health Alert Network (HAN) to state and local health officers, public information officers, epidemiologists, HAN coordinators, and clinician organizations.

Strategies for Implementing Vaccination Recommendations in Health-Care Settings

Successful vaccination programs combine publicity and education for health-care workers and other potential vaccine recipients, a plan for identifying persons at

high risk, use of reminder/recall systems, assessment of practice-level vaccination rates with feedback to staff, and efforts to remove administrative and financial barriers that prevent persons from receiving the vaccine, including use of standing orders programs. Using standing orders programs is recommended for long-term-care facilities (e.g., nursing homes and skilled nursing facilities), hospitals, and home health agencies to ensure the administration of recommended vaccinations for adults. Standing orders programs for both influenza and pneumococcal vaccination should be conducted under the supervision of a licensed practitioner according to a physician-approved facility or agency policy by health-care workers trained to screen patients for contraindications to vaccination, administer vaccine, and monitor for adverse events. The Centers for Medicare and Medicaid Services (CMS) has removed the physician signature requirement for the administration of influenza and pneumococcal vaccines to Medicare and Medicaid patients in hospitals, long-term-care facilities, and home health agencies. To the extent allowed by local and state law, these facilities and agencies may implement standing orders for influenza and pneumococcal vaccination of Medicare- and Medicaid-eligible patients. Other settings (e.g., outpatient facilities, managed care organizations, assisted living facilities, correctional facilities, pharmacies, and adult workplaces) are encouraged to introduce standing orders programs as well. In addition, physician reminders (e.g., flagging charts) and patient reminders are recommended strategies for increasing rates of influenza vaccination. Persons for whom influenza vaccine is recommended can be identified and vaccinated in the settings described in the following sections.

Outpatient Facilities Providing Ongoing Care

Staff in facilities providing ongoing medical care (e.g., physicians' offices, public health clinics, employee health clinics, hemodialysis centers, hospital specialty-care clinics, and outpatient rehabilitation programs) should identify and label the medical records of patients who should receive vaccination. Vaccine should be offered during visits beginning in September and throughout the influenza season. The offer of vaccination and its receipt or refusal should be documented in the medical record. Patients for whom vaccination is recommended and who do not have regularly scheduled visits during the fall should be reminded by mail, telephone, or other means of the need for vaccination.

Outpatient Facilities Providing Episodic or Acute Care

Beginning each September, acute health-care facilities (e.g., emergency departments and walk-in clinics) should offer vaccinations to persons for whom vaccination is recommended or provide written information regarding why, where, and how to obtain the vaccine. This written information should be available in languages appropriate for the populations served by the facility.

Nursing Homes and Other Residential Long-Term--Care Facilities

During October and November each year, vaccination should be routinely provided to all residents of chronic-care facilities with the concurrence of attending physicians. Consent for vaccination should be obtained from the resident or a family member at the time of admission to the facility or anytime afterwards. All residents should be vaccinated at one time, preceding the influenza season.

Residents admitted through March after completion of the vaccination program at the facility should be vaccinated at the time of admission.

Acute-Care Hospitals

Persons of all ages (including children) with high-risk conditions and persons aged ≥ 50 years who are hospitalized at any time during September to March should be offered and strongly encouraged to receive influenza vaccine before they are discharged. In one study, 39 to 46 percent of adult patients hospitalized during the winter with influenza-related diagnoses had been hospitalized during the preceding autumn. Thus, the hospital serves as a setting in which persons at increased risk for subsequent hospitalization can be identified and vaccinated. However, vaccination of persons at high risk during or after their hospitalizations is often not done. In a study of hospitalized Medicare patients, only 31.6% were vaccinated before admission, 1.9 percent during admission, and 10.6 percent after admission. Using standing orders in hospitals increases vaccination rates among hospitalized persons.

Visiting Nurses and Others Providing Home Care to Persons at High Risk

Beginning in September, nursing-care plans should identify patients for whom vaccination is recommended, and vaccine should be administered in the home, if necessary. Caregivers and other persons in the household (including children) should be referred for vaccination.

Other Facilities Providing Services to Persons Aged ≥ 50 Years

Beginning in October, such facilities as assisted living housing, retirement communities, and recreation centers should offer unvaccinated residents and attendees vaccination on-site before the influenza season. Staff education should emphasize the need for influenza vaccine.

Health-Care Workers

Beginning in October each year, health-care facilities should offer influenza vaccinations to all workers, including night and weekend staff. Particular emphasis should be placed on providing vaccinations to persons who care for members of groups at high risk. Efforts should be made to educate health-care workers regarding the benefits of vaccination and the potential health consequences of influenza illness for themselves, their family members, and their patients. All health-care workers should be provided convenient access to influenza vaccine at the work site, free of charge, as part of employee health programs.

Influenza Vaccine Supply

Influenza vaccine distribution delays or vaccine supply shortages have occurred in the United States vaccine in three of the last five influenza seasons. Influenza vaccine delivery delays or vaccine shortages remain possible in part because of the inherent critical time constraints in manufacturing the vaccine given the annual updating of the influenza vaccine strains. Steps being taken to accommodate possible future delays or vaccine shortages include identification

and implementation of ways to expand the influenza vaccine supply and improvement of targeted delivery of vaccine to groups at high risk when delays or shortages are expected.

Influenza Vaccine Use During Shortages of Inactivated Vaccine

The Advisory Committee on Immunization Practices (ACIP) will publish additional guidance regarding the prioritized (tiered) use of inactivated influenza vaccine to be implemented only during periods when there is a shortage of influenza vaccine. Otherwise, when vaccine is in adequate supply, every effort should be made to promote and use influenza vaccine for all regularly targeted groups and for other persons who wish to reduce their risk for influenza illness. The prioritized (tiered) use of influenza vaccine during inactivated influenza vaccine shortages applies only to use of inactivated vaccine and not to LAIV. When feasible, during shortages of inactivated influenza vaccine, LAIV should be used preferentially for all healthy persons aged 5 to 49 years (including health-care workers) to increase the availability of inactivated vaccine for groups at high risk.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Foreign Language Translations
Patient Resources
Resources
Staff Training/Competency Material
Wall Poster

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

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IDENTIFYING INFORMATION AND AVAILABILITY

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Not applicable: The guideline was not adapted from another source.

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Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

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Advisory Committee on Immunization Practices (ACIP)

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The preparers of the guideline report have signed a conflict of interest disclosure that verifies no conflict of interest.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline combined with the addended material, updates a previous version: Centers for Disease Control and Prevention. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2004 May 28;53(RR-6):1-40.

This guideline is updated annually for each upcoming influenza season.

GUIDELINE AVAILABILITY

July 2005 Guideline

Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).

September 2005 Addendum

Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).

January 2006 Addendum

Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Flu gallery: provider education materials for the 2005-06 flu season. Posters, brochures, flyers, buttons and stickers. Available in Spanish and English from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).
- Cover your cough. Printable flyers and posters for use in health care settings. Available in Spanish, Vietnamese, Chinese, Tagalog, and English from the [CDC Web site](#).

PATIENT RESOURCES

The following are available:

- Flu gallery: patient education materials for the 2005-06 flu season. Posters, brochures, flyers, buttons and stickers. Available in Spanish and English from the [Centers for Disease Control and Prevention \(CDC\) Web site](#).
- Patient screening form for inactivated influenza vaccine. Available in Portable Document Format (PDF) from the [CDC Web site](#).
- Influenza vaccine information statements (VISs). Available in Spanish and English from the [CDC Web site](#).
- Fact sheets in other languages. Available in Chinese, French, Japanese, Korean, Spanish, Tagalog, and Vietnamese from the [CDC Web site](#).
- Cover your cough. Printable flyers and posters for use in public settings. Available in Spanish, Vietnamese, Chinese, Tagalog, and English from the [CDC Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

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